REMARKS

The present continuation application, as amended by the instant Preliminary Amendment, conforms the specification and claims to that of parent application, Serial No. 10/006,279, filed December 4, 2001 that was subject to final rejection.

Applicants submit that the present application is patentable over the rejection of record. The final rejection in the parent application was made under 35 U.S.C. §103(a) as being unpatentable over International Publication No. WO 92/01696 to Bateson et al.

The claims currently in this application are novel over Bateson et al. insofar as the acylation step in Bateson et al. occurs by reaction with an ester. The claims of the present application involve acylation by reaction with an acid or a salt of an acid. That the final rejection in the parent application is made under 35 U.S.C. §103(a), and not 35 U.S.C. §102(b), is an implicit admission by the USPTO that this is so.

The grounds advanced in support of the final rejection in the parent application, however, argues that the aforementioned facts are enough to make out a prima facie case of obviousness. Applicants submit that even if that conclusion is true, still the showing of unexpected results, discussed below, rebuts that presumption. Applicants urge that such a showing of unexpected results is presented.

Attention is directed to distinguished step (g) in Example 1 of Bateson et al. That step, which is set forth on Page 39, involves reaction of 2-(Z)-methoxyimino-2-(2-tritylamino-thiazol-4-yl)acetic acid hydrochloride and mesyl chloride. That reaction produces t-butyl (6R, 7R)-7-[2-(Z)-methoxyimino-2-(2-tritylaminothiazol-4-yl)acetamido]-3-tetrahydrofuran-2-yl)-ceph-3-em-4-carboxylate. This ester producing step occurs at a temperature of -40°C.

This difficult reaction, insofar as it occurs at cryogenic temperatures, is essential to produce the ester compound, denoted in Bateson et al. as compound (II), not included in the claimed process of the present application. Rather, an acid compound, denoted by structural formula II in the claims of the present application, permits omission of this difficult synthesis step.

Not only does this Bateson et al. reaction occur at a cryogenic temperature but, in addition, the reaction to produce the ester involves reaction with the acid chloride, mesyl chloride. Those skilled in the art are aware that mesyl chloride is a highly unstable compound that hydrolyzes upon contact with water. As such, the Bateson et al. reaction cannot employ water as solvent or even tolerate small amounts of that desirable solvent.

The synthesis of compounds within the contemplation of formula II of the claims of the present application, on the other hand, are simpler and far less difficult to carry out. Indeed, the synthesis of a typical compound within the generic class of compounds denoted by formula II is described in Example 1, Method A, at Page 27 of the specification of the present application. That reaction, which occurs in aqueous medium, involves reaction of 7-amino-8-oxo-3-(tetrahydrofuran-2-yl)-5-thia-1-aza-bicyclo[4.2.0]octa-1(6),2,4-triene-2-carboxylic acid, a species of generic formula II and a mixture of (Z)-2-amino-α-(methoxyamino)-4-thiazole acetic acid anhydride and O,O-diethyl hydrogen phosphorothioate. These commercially available compounds react under ambient thermodynamic conditions.

These remarks establish that the replacement of the ester of compound II in the process of the present application with the acid of compound II in the claims of the present application represent far more than an obvious replacement of one reactant for another. This

replacement represents a major synthesis advance in the preparation of commercially important 3-cyclic-ether substituted ciphalosporin. As such, the claims of the present application are patentable over the rejection imposed in the parent application.

The above remarks establish the patentable nature of process Claims 1 to 20. Product Claims 21 to 24 are patentable based on the patentable nature of process Claims 1 to 20 of the present application. That the compounds of these claims cannot be prepared by the method taught by Bateson et al. establishes not only their novelty but their unobviousness over Bateson et al.

The above amendment and remarks establish the patentable nature of all the claims currently in this application. Notice of Allowance and passage to issue of these claims, Claims 1 to 24, is therefore respectfully solicited.

Respectfully submitted,

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